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10/755,545	01/12/2004	David Phillips	048501/273281	1302

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EXAMINER	
EMCH, GREGORY S	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/755,545	PHILLIPS ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *8-12,14-20 and 23-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,13,21,22 and 50-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-52* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/04/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence alignments A and B*.

DETAILED ACTION

Response to Amendment

Claims 1, 2, 4, 5, 7 and 47 have been amended and new claims 50-52 were added as requested in the amendment filed on 04 December 2007. Following the amendment, claims 1-52 are pending in the instant application.

Claims 8-12, 14-20 and 23-49 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected subject matter, there being no allowable generic or linking claim. Applicants timely traversed the restriction (election) requirement in Paper filed on 09 March 2007.

Claims 1-7, 13, 21, 22 and 50-52 are under examination in the instant office action.

Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants' response and withdrawn.

This application contains claims 8-12, 14-20 and 23-49 drawn to an invention nonelected with traverse in Paper filed on 09 March 2007. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Election/Restrictions

In the reply filed on 04 December 2007, Applicants request that the Examiner clarify on the record what claims will be rejoined and examined at such time that a

linking claim is found allowable. With the current amendment, claim 1 no longer recites the generic term “activin antagonist" and is no longer a linking claim. Therefore, linking claim practice does not apply to the instant claims.

Information Disclosure Statement

A signed and initialed copy of the IDS paper filed 04 December 2007 is enclosed in this action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection of claims 1-7, 13, 21 and 22 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 5,470,826 is maintained for reasons of record and as set forth below.

In the reply filed on 04 December 2007, Applicants state, "The Examiner is reminded that the '826 patent issued November 28, 1995 and thus the rejection of the claims based on obviousness-type double patenting is improper." Applicants assert that the '826 patent is drawn to polypeptides exhibiting an inhibitory action over follitropin and that said patent provides no information on formulating or for dosage amounts for the use of the polypeptides. Accordingly, Applicants assert that the patent does not anticipate nor render obvious the currently pending claims.

Applicants' arguments have been fully considered and are not found persuasive. Applicants' statement regarding the issue date of the '826 patent is unclear. The Examiner is unable to find any guidance in the MPEP regarding the issue date of a patent as precluding an obviousness-type double patenting rejection. Clarification by

Applicants is requested. Furthermore, it is irrelevant that the '826 patent provides no information on formulating or for dosage amounts for the use of the polypeptide; the instantly pharmaceutical composition comprising the instantly claimed protein are described by the '826 patent. Thus, the claims of the '826 patent are indeed obvious variants of those of the instant application.

The provisional rejection of claims 1-7, 13, 21 and 22 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 87 of copending Application No. 10/318,283 is maintained for reasons of record and as set forth below.

The provisional rejection of claims 1-7, 13, 21 and 22 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 60 of copending Application No. 10/575,049 is maintained for reasons of record and as set forth below.

The provisional rejection of claims 1-7, 13, 21 and 22 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 51 and 57-60 of copending Application No. 10/571,837 is maintained for reasons of record and as set forth below.

In the reply filed on 04 December 2007, Applicants assert that the instant rejections are improper because the present application and the co-pending applications are not commonly owned. Applicants assert that the present application has a filing date of January 12, 2004, which is earlier than the filing date of the

copending applications, and if issued into a patent would expire before the expiration date of a patent issuing from the '283, '049, and ' 837 applications. Thus, Applicants assert that there is no unjust patent term extension. Applicants allege that the with regards to the instant application and the copending applications, "At no time were these two inventions commonly owned." Applicants admit that the present application and the copending applications share a common inventor. Applicants provide a discussion of double patenting form paragraphs provided in MPEP chapter 800, e.g., regarding potential rejections under 35 U.S.C. 102(e) or 102(e)/103(a). Applicants discuss the Create Act and state that the present application and the '283, '049, and '837 applications do not have a common assignee or are not subject to a joint research agreement as defined by The CREATE Act. Applicants allege that the provisions of 35 U.S.C. 103(c) do not apply and that the copending applications are not prior art against the present application. Applicants assert that even if the rejections were proper, the Examiner should allow the earlier filed application to issue. Applicants state, "At which time allowable subject has been agreed upon, and the provisional nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the earlier filed of the pending applications, the Examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer."

Applicants' arguments have been fully considered and are not found persuasive.

It is noted that the full serial number of the '049 application is 10/575,049. The Examiner is aware that the instant application has an earlier U.S. effective filing date than the cited copending applications, that the copending applications and the instant

application are not currently commonly owned and that the copending applications and the instant application share a common inventor. The Examiner has used Chart I-B for conflicting claims between two applications provided in MPEP 804 in formulating the instant provisional double patenting rejections. Since the applications collectively share at least one common inventor but do not collectively share a common assignee, Chart I-B teaches that the Examiner should use form paragraphs 8.33 & 8.35 or 8.37 to provide a provisional obviousness double patenting rejection, which the Examiner has provided in the office action dated 04 June 2007. Since the instant application has the earliest U.S. effective filing date, no provisional rejections under 35 U.S.C. 102(e)/103(a) have been put on the record. Regarding Applicants' comment that the Examiner should allow the earlier filed application to issue without a terminal disclaimer, inasmuch as the current claims are not patentable at this time, the provisional obviousness-type double patenting rejections are properly maintained.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 7 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims ultimately depend from claim 1 and recite the limitation "wherein the activin antagonist is". There is insufficient

antecedent basis for this limitation since claim 1 does not recite "activin antagonist."

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4-6, 13, 21 and 50-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/05998 to Duan et al.

The claims are directed to a pharmaceutical composition for the treatment and/or prophylaxis of disease associated with fibrosis in a vertebrate, said composition comprising follistatin, or a fragment(s) or analogue thereof and wherein said follistatin is present in an amount of from 0.001% to 5% w/v of the composition.

The '998 document teaches a follistatin polypeptide that is 100% identical to the instant SEQ ID NO: 1, (see attached Sequence alignment A) and fragments, analogues and derivates thereof (pp.6-7 and 48-54), as in claims 1, 2, 4-6, 13, 21 and 50-52. The '998 application teaches pharmaceutical compositions comprising the polypeptide and pharmaceutically acceptable carriers, adjuvants or diluents (pp.94-95), as in claim 1. The '998 document teaches that the follistatin protein binds to and antagonizes activin (p.1), as in claim 13. The reference teaches that the pharmaceutical compositions are useful to treat reproductive disorders, cancers and other cellular growth and differentiation disorders (p.8), i.e. hyperproliferative disorders, as in claim 21.

The '998 document does not the amount of follistatin in the pharmaceutical composition as in claims 1 and 50-52. However, in the instant case this is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize (see MPEP 2144.05). Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal in the claimed composition. Thus, absent some demonstration of unexpected results from the claimed

parameters, this optimization of constants would have been obvious at the time of Applicants' invention.

It is noted that the limitations of "a pharmaceutical composition for the treatment and/or prophylaxis of disease associated with fibrosis in a vertebrate" in claim1, of "wherein the disease associated with fibrosis is one of: a hyperproliferative or inflammatory fibrotic disease; a pulmonary fibrosis; an inflammatory bowel disease, or a related condition such as ulcerative colitis or Crohn's Disease; or liver fibrosis or cirrhosis" in claim 21, and of "wherein the disease associated with fibrosis is liver fibrosis or cirrhosis" in claim 22 are directed to the preamble of claim 1 and thus impart no patentable weight on the claim (see MPEP 2111.02, section II). Therefore, it is irrelevant that the reference did not appreciate the remaining intended purposes of the claimed compositions.

Claims 1, 2, 5-7, 13, 21, 22 and 50-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/10364 A1 to Ruben et al.

The claims are directed to a pharmaceutical composition for the treatment and/or prophylaxis of disease associated with fibrosis in a vertebrate, said composition comprising follistatin, or a fragment(s) or analogue thereof, and wherein said follistatin is present in an amount of from 0.001% to 5% w/v of the composition.

The '364 document teaches a follistatin polypeptide that is 100% identical to the instant SEQ ID NO: 2, (see attached Sequence alignment B) and fragments, analogues and derivates thereof (pp.5-6, 34-36, 52 and 53), as in claims 1, 2, 5-7, 13, 21, 22 and

50-52. The '364 application teaches pharmaceutical compositions comprising the polypeptide and pharmaceutically acceptable carriers, adjuvants or diluents (pp.59-62), as in claim 1. The '364 document teaches that the follistatin protein binds to and antagonizes activin (p.28), as in claim 13. The reference teaches that the pharmaceutical compositions are useful to treat reproductive disorders, cancers and other cellular growth and differentiation disorders (p.7), i.e. hyperproliferative disorders, as in claim 21.

The '364 document does not the amount of follistatin in the pharmaceutical composition as in claims 1 and 50-52. However, in the instant case this is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize (see MPEP 2144.05). Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal in the claimed composition. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of constants would have been obvious at the time of Applicants' invention.

It is noted that the limitations of "a pharmaceutical composition for the treatment and/or prophylaxis of disease associated with fibrosis in a vertebrate" in claim1, of "wherein the disease associated with fibrosis is one of: a hyperproliferative or inflammatory fibrotic disease; a pulmonary fibrosis; an inflammatory bowel disease, or a related condition such as ulcerative colitis or Crohn's Disease; or liver fibrosis or cirrhosis" in claim 21, and of "wherein the disease associated with fibrosis is liver

fibrosis or cirrhosis" in claim 22 are directed to the preamble of claim 1 and thus impart no patentable weight on the claim (see MPEP 2111.02, section II). Therefore, it is irrelevant that the reference did not appreciate the remaining intended purposes of the claimed compositions.

Claims 1, 2, 3, 5, 13, 21, 22 and 50-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,041,538 to Ling et al.

The claims are directed to a pharmaceutical composition for the treatment and/or prophylaxis of disease associated with fibrosis in a vertebrate, said composition comprising follistatin, or a fragment(s) or analogue thereof, and wherein said follistatin is present in an amount of from 0.001% to 5% w/v of the composition.

The '538 patent teaches pharmaceutical compositions comprising follistatin combined with a pharmaceutically acceptable carrier (col.10, lines 1-3), as in claims 1, 2, 5, 13, 21, 22 and 50-52. Although the '538 patent does not appreciate that the follistatin protein binds to and antagonizes activin as in claim 13, this is nonetheless an inherent property of said protein. Applicants are reminded that chemical compounds and their properties are inseparable (In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA1963)), as are their processes and yields (In re Von Schickh, 362 F.2d 821, 150 USPQ 300 (CCPA 1966)). It is noted that the limitations of "a pharmaceutical composition for the treatment and/or prophylaxis of disease associated with fibrosis in a vertebrate" in claim1, of "wherein the disease associated with fibrosis is one of: a hyperproliferative or inflammatory fibrotic disease; a pulmonary fibrosis; an inflammatory

bowel disease, or a related condition such as ulcerative colitis or Crohn's Disease; or liver fibrosis or cirrhosis" in claim 21, and of "wherein the disease associated with fibrosis is liver fibrosis or cirrhosis" in claim 22 are directed to the preamble of claim 1 and thus impart no patentable weight on the claim (see MPEP 2111.02, section II). Therefore, it is irrelevant that the reference did not appreciate the intended purpose of the claimed compositions. The '538 patent teaches that the follistatin proteins of the invention (follistatin A, which has 315 amino acids and follistatin B, which has 288 amino acids) are single chains, have molecular weights of approximately 35,000 Daltons and 32,000 Daltons, respectively (as estimated by SDS-PAGE), were isolated from follicular fluid and are able to inhibit FSH (col.1, lines 20-24 and 40-68, col.7, lines 11-14 and 64) as in claim 3.

The '538 patent does not the amount of follistatin in the pharmaceutical composition as in claims 1 and 50-52. However, in the instant case this is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize (see MPEP 2144.05). Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal in the claimed composition. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of constants would have been obvious at the time of Applicants' invention.

In the reply filed on 04 December 2007 regarding the previous rejection under 35 U.S.C. 102(b), Applicants assert that the '538 patent discloses the isolation of follistatin

315 and 288, and the prophetic use of these molecules for decreasing fertility/spermatogenesis in female/male mammals. Applicants allege that the patent suggests a dosage of from about 0.1 to about 1 mg per kg of body weight for administration on a regular basis as a male contraceptive and that there is no data, either in vivo or in vitro, to support the suggested use let alone the suggested dosage rates.

Applicants' arguments have been fully considered and are not found persuasive for the reasons set forth above with respect to optimization of parameters. Given the teachings of pharmaceutical compositions of the '538 patent and given the level of skill in the art, it would have been obvious for the artisan optimize the concentration of follistatin for inclusion in the pharmaceutical composition as claimed.

Conclusion

No claims are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregory S. Emch/

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17 March 2008

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